by excess chromic acid in glacial acetic acid as described by Bilz.[6] Olefin dibromides were first heated with zinc dust in glacial acetic acid. The zinc and zinc bromide were removed by filtration of the cooled solution before the chromic acid was added. The product of oxidation isolated was either 4,4'-dibromobenzophenone, m. p. 173–174°, or *p*-bromobenzoic acid, m. p. 254–255°, in yields of 50% or higher. Direct oxidation of α,α',4,4'-tetrabromobibenzyl gave a 91% yield of 4,4'-dibromobenzil,[7] m. p. 228°.

The Reaction of Bromine with Tetrakis-(*p*-bromophenyl)-ethylene.—A 1.00-g. sample of the tetrabromide was placed in a desiccator in which the atmosphere was saturated with bromine vapor. The green, powdery product weighed 1.32 g. After standing for several hours the solid product was nearly white and weighed 0.99 g. When this sample was left several days in an atmosphere containing bromine vapor at a much lower concentration than that of air saturated with bromine vapor, the solid product was slightly green and weighed only 1.05 g. Again standing yielded a white product. After crystallization from chloroform–ethanol the m. p. was 258–259°.

1,1-Dibromo-2,2-diphenylethylene.—A solution of 3.6 g. (0.020 mole) of 1,1-diphenylethylene in 20 ml. of glacial acetic acid was treated with 2.2 ml. (0.043 mole) of bromine. The solution became warm and the color rapidly faded. Heating the mixture partially restored the bromine color and caused a rapid evolution of hydrogen bromide. The color faded again during the heating process. When hydrogen bromide was no longer evolved, about 40 g. of ice and water was added to the reaction mixture. The 6.5-g. yield of crude product was crystallized from 95% ethanol to yield 4.1 g. (61%) of 1,1-diphenyl-2,2-dibromoethylene, m. p. 83–84° which is the m. p. reported.[8]

Summary

1. Twenty solid aromatic compounds reacted with bromine vapor to yield products in which the *p*-positions of unsubstituted phenyl groups had brominated and in which olefinic double bonds, not highly substituted, had added bromine.

2. These reactions of bromine vapor with solid aromatic compounds have been explained as involving ionic intermediates in which a molecule of the aromatic compound and one or more bromine molecules are combined in either an absorbed phase or in a film of solution on the surface of the solid. Subsequent reactions of the intermediates explain the products which have been observed.

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[6] Bilz, *Ann.*, **296**, 219 (1897).

[7] Bilz, *Ber.*, **41**, 1761 (1908).

[8] Harris and Frankforter, THIS JOURNAL, **48**, 3144 (1926).

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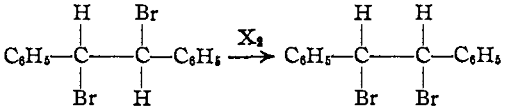
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE STATE UNIVERSITY OF IOWA]

The Reactions of the α,α'-Dibromobibenzyls and the α,α'-Dichlorobibenzyls with Halogens[1]

BY ROBERT E. BUCKLES, WALTER E. STEINMETZ[2] AND NORRIS G. WHEELER

The *cis–trans* isomerization of olefins by the action of halogen atoms is well known.[3] A similar isomerization has now been observed in the conversion of *dl*-α,α'-dibromobibenzyl to the *meso*-isomer by the action of halogens.



$$C_6H_5-\underset{Br}{\overset{H}{C}}-\underset{H}{\overset{Br}{C}}-C_6H_5 \xrightarrow{X_2} C_6H_5-\underset{Br}{\overset{H}{C}}-\underset{Br}{\overset{H}{C}}-C_6H_5$$

The isomerization took place in good yield when solid *dl*-dibromide was left in contact with bromine vapor for two weeks or when a carbon tetrachloride solution of the *dl*-dibromide was treated with bromine or iodine for several days at room temperature. A carbon tetrachloride solution of the *dl*-dibromide containing chlorine gave the *meso*-dibromide, but only in 20% yield. The reaction of chlorine with either *dl*- or *meso*-dibromobibenzyl in sunlight gave α-bromo-α'-chlorobibenzyl plus other dihalides and trihalides. These reactions were not observed when the reactions were carried out in absolute darkness except when bromine vapor reacted with the solid dibromide.

A similar isomerization of *dl*-α,α'-dichlorobibenzyl was brought about in sunlight by the action of chlorine or bromine in carbon tetrachloride, but it was impossible to ascertain to what extent this reaction took place. Both the *meso*- and *dl*-dichlorides reacted with chlorine or bromine to give mixtures of halogenated products. Only a small amount of *meso*-dichlorobibenzyl could be isolated from either the chlorination or bromination of the *dl*-isomer. The *dl*-dichloride was recovered in high yield from the reaction with iodine in sunlight. The reaction of either *meso*- or *dl*-α,α'-dichlorobibenzyl with chlorine gave rise to a number of chlorination products: α,α,α'-trichlorobibenzyl, α,α,α',α'-tetrachlorobibenzyl and benzotrichloride. No evidence of ring chlorination could be found. Bromine reacted with *dl*-dichlorobibenzyl to give trihalides as well as dihalides while the *meso*-isomer gave mostly starting material.

The results all indicate that halogen replaces bromine from the *dl*-dibromide probably by way of halogen atoms. When the displacing halogen is not bromine, the bromine atom which is removed could effect a displacement of the new

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[1] Abstracted in part from two theses presented to the Graduate College of the State University of Iowa by Walter E. Steinmetz in partial fulfillment of the requirements for the Ph.D. degree and by Norris G. Wheeler in partial fulfillment of the requirements of the M.S. degree. Part of this paper was presented before the Organic Division of the American Chemical Society, San Francisco, March 30, 1949.

[2] Allied Chemical and Dye Fellow, 1946–1947.

[3] Price, "Reactions at Carbon-Carbon Double Bonds," Interscience Publishing Co., New York, N. Y., Chap. 3, 1946.

halogen with the result that dibromide would be formed. The isomerization of the *dl*-dichloride could be explained the same way. Such replacements of one halogen for another by means of atoms or molecules are not unknown. The chlorination and bromination of methylene iodide are reported[4] to give methylene chloride and methylene bromide, respectively. More recently the exchange of radioactive iodine with alkyl iodides has been investigated and found to involve iodine atoms replacing iodine atoms bonded to carbon.[5]

During the halogenation of *dl*-dibromobibenzyl isomerization involving displacement of bromine is the more important reaction except, possibly, in the reaction with chlorine where appreciable substitution was observed as well as displacement. On the other hand, during the halogenation of α,α'-dichlorobibenzyl it is more likely that halogen will be substituted for hydrogen on the open chain portion of the molecule than that chlorine will be displaced by halogen. It is especially significant that iodine, which would not be expected to substitute efficiently for hydrogen, gave no reaction with either of the dichlorides but isomerized the *dl*-dibromide in good yield. Evidently the carbon–chlorine bond is too stable for a displacement to take place easily as compared to the substitution of halogen for hydrogen. On the other hand the carbon–bromine bond would be less stable to such a change and would be more likely to break than the carbon–hydrogen bond under the influence of the incoming halogen atom. Besides this the presence of the larger, more bulky bromine atoms in a dibromobibenzyl seems to lessen the tendency for substitution on the open chain portion of the molecule as compared with a dichlorobibenzyl. Such substitution would lead to compounds with three and four halogens on the open chain portions of the molecules. Only two such compounds in which two or more of the halogen atoms are bromine have been described: α-chloro-α,α'-dibromobibenzyl[6] and α,α,α'-tribromobibenzyl.[7] The former is reported to decompose at its m. p. (127°) and the latter is reported to give off hydrogen bromide when heated. Such instability indicates that the presence of two or more bromine atoms in these trihalides, and presumably in the tetrahalides, decreases the stability of the molecules. The well known resistance of the double bond of α,α'-dibromostilbene to bromine addition also bears out this point. Evidently the steric hindrance of the bromine atoms plus that of the benzene rings can operate either to keep the polyhalides from being formed or to labilize them with respect to elimination of hydrogen halide or halogen.

The reaction of bromine vapor with solid *dl*-dibromide probably takes place by means of the action of bromine molecules or ions in an adsorbed phase on the surface of the crystals. The nature of this reaction mechanism is as yet obscure, but the fact that the reaction proceeds in the dark indicates that free radical intermediates probably are not formed.[8]

The nature of the displacement reactions involved in the above mechanisms would not matter since the stable dihalo compound would be the one formed eventually whether a Walden inversion is involved with each replacement or not. Further work on the possibility that displacement by halogen atoms is accompanied by Walden inversion is continuing in this Laboratory.

Experimental

***cis*-Stilbene.**—The decarboxylation of 12.0 g. of α-phenylcinnamic acid in 120 ml. of quinoline in the presence of 1 g. of copper chromite at 215° gave an 85% yield of *cis*-stilbene of b. p. 134° (10 mm.).[9]

***dl*-α,α'-Dibromobibenzyl.**—The addition of 1.2 ml. of bromine to 3.0 g. of *cis*-stilbene in 30 ml. of carbon disulfide kept cold and in the dark yielded 83% of the *dl*-dibromobibenzyl along with 0.5 g. of the *meso* isomer. The *dl* isomer had m. p. 110–111°[10] from ethanol.[11]

α,α'-Dichlorobibenzyls.—The treatment of 10 g. of *trans*-stilbene with 300 ml. of a saturated solution of chlorine in anhydrous ether in sunlight or ultraviolet light for five hours yielded a mixture of *dl*- and *meso*-α,α'-dichlorobibenzyl.[12] The total yield of both isomers was 55%: 4.7 g. of the *dl*-dichloride, m. p. 89–91° from ligroin, and 3.0 g. of the *meso* isomer, m. p. 189–191° from ethanol.

α-Chlorostilbene.—The treatment of 35 g. of molten desoxybenzoin with 40 g. of phosphorus pentachloride gave a 14.7 g. (38%) yield of α-chlorostilbene, m. p. 50–51° from ethanol.[6]

α,α,α'-Trichlorobibenzyl.—A solution of α-chlorostilbene in 20 ml. of carbon tetrachloride saturated with chlorine was allowed to stand half an hour in the dark at 0°.[6] A yield of 4.4 g. (66%) of the trichloride of m. p. 102–103° was obtained by recrystallization from acetic acid.

$\alpha,\alpha,\alpha',\alpha'$-Tetrachlorobibenzyl.—A solution of 15 g. of benzotrichloride in 30 ml. of benzene was treated with 45 g. of copper powder.[13] A 16% yield (2.0 g.) of the tetrachloride of m. p. 161° was obtained after crystallization from benzene.

Elimination of Halogen from the Halides by Zinc Dust.—A mixture of 1.0 g. of the halide in 20 ml. of glacial acetic acid and excess zinc dust was boiled under reflux for three hours. The zinc was removed by filtration, and the filtrate was poured into 80 ml. of water. The solid which precipitated was recrystallized from 95% ethanol. Treatment of $\alpha,\alpha,\alpha',\alpha'$-tetrachlorobibenzyl yielded 0.20 g. of *trans*-α,α'-dichlorostilbene, m. p. 139°, and 0.10 g. of *cis*-α,α'-dichlorostilbene, m. p. 60–62°.[14] The elimination of chlorine from α,α,α'-trichlorobibenzyl gave a 69% yield (0.52 g.) of α-chlorostilbene, m. p. 48–50°. An 86% yield (0.60 g.) of *trans*-stilbene of m. p. 123° was obtained from *meso*-α,α'-dichlorobibenzyl.

Isomerization of Solid *dl*-α,α'-Dibromobibenzyl by Bromine Vapor.—Four grams of *dl*-dibromobibenzyl was allowed to stand in a bromine atmosphere for two weeks.[8] During this time it became somewhat brown but remained

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[4] Butlerow, *Ann.*, **111**, 242 (1859); *Z. Chem.*, **5**, 276 (1869).

[5] Noyes, THIS JOURNAL, **70**, 2614 (1948).

[6] Sudborough, *J. Chem. Soc.*, **71**, 218 (1897).

[7] Limpricht and Schwanert, *Ann.*, **145**, 330 (1868).

[8] Buckles, Hausman and Wheeler, THIS JOURNAL, **72**, 2494 (1950).

[9] Taylor and Crawford, *J. Chem. Soc.*, 1130 (1934).

[10] All melting points are corrected.

[11] Wislicenus, *Chem. Zentr.*, **72**, I, 463 (1901).

[12] Pfeiffer, *Ber.*, **45**, 1816 (1912).

[13] Hanhart, *ibid.*, **15**, 90 (1882).

[14] Marckwald and Karczag, *ibid.*, **40**, 2994 (1907).

solid. The solid was crystallized from benzene to give 3.6 g. (90%) of *meso*-α,α'-dibromobibenzyl, m. p. 234–235°; the mixed m. p. with an authentic sample showed no depression. All m. p.'s of the *meso*-dibromide were taken in a melting point bath preheated to 210° or higher before the sample tube was inserted.

A similar experiment was carried out with 0.50 g. of the *dl*-dibromide in a bromine atmosphere in absolute darkness. A 0.35 g. (70%) yield of the *meso* isomer was obtained by recrystallization from benzene.

Isomerization of *dl*-α,α'-Dibromobibenzyl by Bromine or Iodine in Carbon Tetrachloride.—A solution of 0.50 g. of the *dl*-dibromide and 0.25 ml. of bromine in 10 ml. of carbon tetrachloride was allowed to stand in diffuse daylight for seven days. The solution was then evaporated to dryness, and the residue was recrystallized from benzene. The product was 0.40 g. (80%) of *meso*-dibromobibenzyl. An identical reaction was carried out for three days replacing the bromine with a few iodine crystals. The reaction mixture was treated as in the case of bromine reaction. The yield was 0.40 g. (80%) of the *meso* isomer.

Isomerization of *dl*-α,α'-Dibromobibenzyl by Chlorine.—A solution of 2.0 g. of the *dl*-dibromide in 15 ml. of carbon tetrachloride was saturated with chlorine. It was allowed to stand four days in diffuse light. By the end of the second day the solution had turned a dark brown, bromine color. Evaporation of the solution led to a sticky, semisolid residue. Crystallization from carbon tetrachloride and then from benzene yielded 0.40 g. (20%) of the *meso*-dibromide. No other solid product could be isolated from the reaction mixture. The crude product, with carbon tetrachloride completely removed, gave a positive test for chlorine as well as for bromine.

In another experiment a solution of 3.0 g. for *dl*-dibromobibenzyl in 50 ml. of carbon tetrachloride was saturated with chlorine. It was allowed to stand in direct sunlight for one hour. A bromine color appeared and hydrogen halide was evolved. The solution was decolorized by aqueous sodium bisulfite, washed with water, and evaporated. The residue was crystallized from ethanol and 0.23 g. of crude crystals were obtained which after three recrystallizations from ethanol yielded 0.12 g. of α-bromo-α'-chlorobibenzyl, m. p. 222–224°, no lowering when mixed with an authentic sample. An authentic sample of α-bromo-α'-chlorobibenzyl, m. p. 223–224°, was prepared in 92% yield by the action of 5 ml. of stannic chloride on 0.55 g. of *meso*-α,α'-dibromobibenzyl in 70 ml. of benzene.[15] The mother liquor from the first crystallization of the bromochloride was evaporated to dryness. The residue was treated with zinc in acetic acid as described above. Recrystallization from ethanol several times yielded 0.9 g. of *trans*-stilbene, m. p. 121°. The mother liquor from the first crystallization of the stilbene gave a small amount (0.1 g.) of a low melting solid which after two recrystallizations from ethanol yielded α-chlorostilbene, m. p. 48–49°.

Chlorination of *meso*-α,α'-Dibromobibenzyl.—A solution of 0.6 g. of *meso*-dibromobibenzyl in 350 ml. of carbon tetrachloride was saturated with chlorine gas and placed in direct sunlight. By the end of one hour the solution which was originally green due to dissolved chlorine was colorless. The solution was again saturated with chlorine and placed in sunlight. The solution again became colorless and hydrogen halide was evolved. The solution was shaken with aqueous sodium bisulfite and washed with water. The carbon tetrachloride was removed by heating on a steam-bath. The white crystals that remained were recrystallized from ethyl alcohol and gave 0.2 g. of α-bromo-α'-chlorobibenzyl, m. p. 222–223°.

Stability of *dl*-α,α'-Dibromobibenzyl.—Solid *dl*-dibromide in an evacuated desiccator filled with iodine vapor, chlorine gas or hydrogen bromide gas was allowed to stand several days. The dibromide was recovered unchanged in each case. A carbon tetrachloride solution of the *dl*-dibromide saturated with dry hydrogen bromide gas gave no isomerization in seven days. All of the isomerization reactions with halogen in carbon tetrachloride described above when run in total darkness gave virtually quantitative yields of unchanged *dl*-dibromide as the product. A solution of the *dl*-dibromobibenzyl in carbon tetrachloride stood for eighty days in diffuse daylight. The unchanged *dl*-dibromide was isolated quantitatively from the solution.

Chlorination of *dl*-Dichlorobibenzyl.—A solution of 5.0 g. of *dl*-dichlorobibenzyl in 50 ml. of carbon tetrachloride was saturated with chlorine and allowed to stand in direct sunlight for three hours. A good deal of hydrogen chloride was evolved during the reaction. The solution was evaporated, and the residue was crystallized to yield a solid of m. p. 85–90°. Five recrystallizations from ethanol gave 0.5 g. of α,α,α'-trichlorobibenzyl, m. p. 101–103°. The second fraction from the crystallization of the reaction product weighed 0.038 g. after five recrystallizations from ethanol and had m. p. 150–151°. This fraction proved to be a mixture of *meso*-α,α'-dichlorobibenzyl with a little $\alpha,\alpha,\alpha',\alpha'$-tetrachlorobibenzyl. The two compounds could not be separated, but elimination of chlorine with zinc as described above yielded 0.009 g. of *trans*-stilbene (m. p. 120–121°) and 0.005 g. of a mixture of *cis*- and *trans*-α,α'-dichlorostilbene of m. p. 88–94°. A third fraction from the chlorination reaction mixture had m. p. 65–70° and was obtained in 2.4-g. yield. Elimination of chlorine from this fraction yielded 0.60 g. of *trans*-stilbene and 0.14 g. of α-chlorostilbene. These two compounds were identified by m. p. and mixed m. p.

When the photochemical chlorination of *dl*-α,α'-dichlorobibenzyl was carried out as above for three days, distillation of the reaction product at reduced pressure yielded benzotrichloride, b. p. 115–130° (27 mm.). Hydrolysis of the distillate with 10% sodium hydroxide yielded benzoic acid, m. p. 121°.

Chlorination of *meso*-α,α'-Dichlorobibenzyl.—A suspension of 7.0 g. of *meso*-dichlorobenzyl in 90 ml. of carbon tetrachloride was saturated with chlorine and placed in direct sunlight for four hours. During the reaction period the dichloride went into solution, and a large amount of hydrogen chloride was evolved. The solution was then evaporated to dryness. No well-defined crystals could be isolated from the residue. Elimination of chlorine from the residue by zinc dust was carried out as in the case of the chlorination of the *dl*-dichloride. From the elimination reaction were isolated 1.30 g. of *trans*-stilbene, m. p. 123°, 0.10 g. of *trans*-α,α'-dichlorostilbene, m. p. 139°, and 0.14 g. of α-chlorostilbene, m. p. 50°. These products were crystallized several times and identified by m. p. and mixed m. p.

A photochemical chlorination of *meso*-dichlorobibenzyl carried out for three days yielded benzotrichloride as in the case of the *dl*-dichloride. In another experiment the chlorination product was treated with zinc to eliminate chlorine, and 1.5 g. of the crude elimination product was oxidized in 30 ml. of acetone with an excess amount of potassium permanganate. Purification of the reaction product yielded 0.7 g. of benzoic acid, m. p. 121°, and 0.2 g. of benzil, m. p. 94°. No oxidation products with chlorine on the benzene ring could be isolated.

Bromination of *dl*-α,α'-Dichlorobibenzyl.—A solution of 4.00 g. of *dl*-dichlorobibenzyl and 1.56 g. of bromine in 20 ml. of carbon tetrachloride was placed in direct sunlight for two hours. Some hydrogen halide was evolved. The reaction mixture was washed with aqueous sodium bisulfite and with water. The carbon tetrachloride solution was evaporated. The residue yielded 0.10 g. of *meso*-α,α'-dichlorobibenzyl, m. p. 190–191°, after five recrystallizations from ethanol. A second fraction, m. p. 86°, 0.39 g., gave *trans*-stilbene and a mixture of m. p. 44–73°, when treated with zinc in acetic acid. A third fraction, 2.20 g., gave 0.42 g. of *trans*-stilbene, m. p. 121,° and 0.10 g. of α-chlorostilbene, m. p. 46°, when treated with zinc. These products were identified by mixed m. p.

Bromination of *meso*-α,α'-Dichlorobibenzyl.—A mixture of 6.00 g. of *meso*-dichloride and 1.56 g. of bromine in 60 ml. of carbon tetrachloride was placed in direct sunlight for two hours. A limited evolution of hydrogen halide was observed. The reaction mixture was treated as in the

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(15) Pfeiffer and Eistert, *J. prakt. Chem.*, **124**, 168 (1930).

case of the bromination of *dl*-dichloride. The crude reaction product gave a 73% yield of starting dichloride, m. p. 189–190° on recrystallization from ethanol. The only other product was an oil which yielded an oily mixture when treated with zinc in acetic acid. No crystals could be isolated from these oily products.

The Stability of the α,α'-Dichlorobibenzyls.—Solutions of both dichlorobibenzyls in carbon tetrachloride containing iodine gave virtually quantitative yields of the starting dichlorides after standing in direct sunlight for ten days. Starting material was recovered in high yields when carbon tetrachloride solutions of either dichlorobibenzyl were treated with chlorine, bromine or iodine in the dark for as long as ninety-five days.

Chlorination of α,α,α'-Trichlorobibenzyl.—A solution of 0.5 g. of the trichloride in 30 ml. of carbon tetrachloride was saturated with chlorine and placed in direct sunlight for two hours. Crystallization of the product from the oily residue yielded 0.20 g. of $\alpha,\alpha,\alpha'\alpha'$-tetrachlorobibenzyl, m. p. 160°. An oily by-product with a camphor-like odor was also observed.

Summary

1. Bromine vapor has been found to bring about an isomerization of solid *dl*-α,α'-dibromobibenzyl to the *meso*-isomer in 90% yield, both in the dark and in daylight. Bromine and iodine in carbon tetrachloride effected the isomerization of *dl*-dibromobibenzyl in light with high yields. Chlorine gave a much lower yield of the *meso*-isomer and a mixture of products containing trihalides.

2. Chlorine and bromine have been found to isomerize *dl*-α,α'-dichlorobibenzyl to the *meso*-isomer in sunlight, but only very small yields of the *meso*-isomer could be isolated. Several other halogenation products were detected. Iodine did not affect the *meso*- or *dl*-dichlorobibenzyl in sunlight.

3. Displacement of one halogen by another is evidently the preferred reaction during the halogenation of the dibromobibenzyls while with the dichlorobibenzyls substitution of halogen for hydrogen predominates.

4. A mode of isomerization of *dl*-α,α'-dihalobibenzyl involving a series of displacements of one halogen atom for another until the more stable *meso*-α,α'-dihalobibenzyl is formed has been suggested.

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[CONTRIBUTION FROM THE RADIOACTIVITY CENTER OF THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY AND THE MEDICAL LABORATORIES OF THE COLLIS P. HUNTINGTON MEMORIAL HOSPITAL, MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS]

Synthesis of C-14 Carboxyl-labeled Tyrosine and Diiodotyrosine[1]

BY ROBERT BERNER LOFTFIELD

When carboxyl-labeled tyrosine and diiodotyrosine were required for certain studies of animal metabolism, a survey of the available literature revealed no synthesis of tyrosine which could reasonably be adapted to the preparation of carboxyl-labeled tyrosine. Erlenmeyer's[2,3] classic syntheses involve the preparation of either hippuric acid or phenylalanine followed by several reactions whose comparatively poor yields are not easily improved.

Accordingly the much more direct approach, that of the Strecker synthesis, was tried. The required aldehyde, *p*-hydroxyphenylacetaldehyde, is so sensitive that it is known only as its *p*-nitrophenylhydrazone. In this investigation the corresponding methyl ether was prepared by the Darzens[4] aldehyde synthesis using conditions differing from those used by Rosenmund and Dornsaft.[5] Anisaldehyde was treated with ethyl chloroacetate in a solution of sodium in a mixture of ethanol and methanol. The mixed alcohols gave a mixed ester which stays in solution during the subsequent extractions and hydrolysis. The ester was hydrolyzed almost instantaneously by a solution of sodium hydroxide in methanol and ether to give sodium *p*-methoxyphenylglycidate hemihydrate.

Treatment of this salt with weak acids gave the expected aldehyde. However, this aldehyde was always accompanied by varying quantities of resin, even immediately after distillation. Hence, the sodium glycidate was decomposed by dissolving it in a hot solution of sodium bisulfite in water. On cooling, pure stable *p*-methoxyphenylacetaldehyde–sodium bisulfite separated in 56% over-all yield.

The Strecker synthesis and various modifications of it were investigated in order to prepare tyrosine. The only substance which could be isolated was apparently the imino-compound, bis-(α-cyano-β-*p*-methoxyphenylethyl)-amine (m. p. 112–113°). Erlenmeyer[3] had had similar difficulty with the preparation of phenylalanine.

However, excellent results were obtained with the Bucherer[6] hydantoin synthesis which, followed by hydrochloric acid hydrolysis at 140–160°, gave tyrosine in an over-all yield of about 65% based on cyanide.[7] Since the yield based on anisaldehyde is more than 35%, the scheme may find application in the preparation of ordinary synthetic *dl*-tyrosine.

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[1] This research was supported in part by U. S. Navy Contract N5 ori-76; and by an institutional grant from the American Cancer Society to the Massachusetts General Hospital. The C-14 was supplied by the Atomic Energy Commission. Publication No. 701 of the Cancer Commission of Harvard University.

[2] Erlenmeyer and Halsey, *Ann.*, **307**, 138 (1899).

[3] Erlenmeyer and Lipp, *ibid.*, **219**, 161 (1883).

[4] Darzens, *Compt. Rend.*, **139**, 1214 (1904).

[5] Rosenmund and Dornsaft, *Ber.*, **52**, 1740 (1919).

[6] Bucherer, *et al.*, *J. prakt. Chem.*, [2] **140**, 291; **141**, 5 (1934).

[7] Prepared from potassium, ammonia and $C^{14}O_2$ as described earlier; "Nucleonics," Vol. I, No. 3, p. 54 (1947).